Complete Summary

GUIDELINE TITLE

Staging of testicular malignancy.

BIBLIOGRAPHIC SOURCE(S)

Choyke PL, Bluth EI, Bush WH Jr, Casalino DD, Francis IR, Jafri SZ, Kawashima A, Papanicolaou N, Rosenfield AT, Sandler CM, Segal AJ, Tempany C, Resnick MI, Expert Panel on Urologic Imaging. Staging of testicular malignancy. [online publication]. Reston (VA): American College of Radiology (ACR); 2005. 6 p. [57 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Resnick MI, Amis ES Jr, Bigongiari LR, Bluth EI, Bush WH Jr, Choyke PL, Fritzsche PJ, Holder LE, Newhouse JH, Sandler CM, Segal AJ, Rutsky EA. Staging of testicular malignancy. American College of Radiology. ACR Appropriateness Criteria. Radiology. 2000 Jun;215 Suppl:741-6.

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Testicular cancer

GUIDELINE CATEGORY

Evaluation

CLINICAL SPECIALTY

Nuclear Medicine
Oncology
Radiology
Urology

INTENDED USERS

Health Plans
Hospitals
Managed Care Organizations
Physicians
Utilization Management

GUIDELINE OBJECTIVE(S)

To evaluate the appropriateness of initial radiologic examinations for patients with testicular cancer

TARGET POPULATION

Patients with testicular cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. Computed tomography (CT)
    - Abdomen and pelvis
    - Chest
2. X-ray
    - Chest
    - Abdomen, kidneys, ureters, bladder (KUB)
    - Kidney, intravenous urography (IVU), intravenous pyelogram (IVP)
3. Magnetic resonance imaging (MRI), abdomen and pelvis
4. Fluorodeoxyglucose positron emission tomography (FDG PET)
5. Nuclear medicine (NUC), bone scan
6. Invasive (INV), abdomen and pelvis, lymphangiography, bipedal
7. Ultrasound (US)
    - Scrotum
    - Abdomen, retroperitoneal

MAJOR OUTCOMES CONSIDERED

Utility of radiologic examinations in staging of testicular malignancy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches of peer-reviewed medical journals, and the major applicable articles were identified and collected.

NUMBER OF SOURCE DOCUMENTS

The total number of source documents identified as the result of the literature search is not known.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

One or two topic leaders within a panel assume the responsibility of developing an evidence table for each clinical condition, based on analysis of the current literature. These tables serve as a basis for developing a narrative specific to each clinical condition.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Since data available from existing scientific studies are usually insufficient for meta-analysis, broad-based consensus techniques are needed for reaching agreement in the formulation of the appropriateness criteria. The American College of Radiology (ACR) Appropriateness Criteria panels use a modified Delphi technique to arrive at consensus. Serial surveys are conducted by distributing questionnaires to consolidate expert opinions within each panel. These questionnaires are distributed to the participants along with the evidence table

and narrative as developed by the topic leader(s). Questionnaires are completed by the participants in their own professional setting without influence of the other members. Voting is conducted using a scoring system from 1 to 9, indicating the least to the most appropriate imaging examination or therapeutic procedure. The survey results are collected, tabulated in anonymous fashion, and redistributed after each round. A maximum of three rounds is conducted and opinions are unified to the highest degree possible. Eighty percent agreement is considered a consensus. This modified Delphi technique enables individual, unbiased expression, is economical, easy to understand, and relatively simple to conduct.

If consensus cannot be reached by this Delphi technique, the panel is convened and group consensus techniques are utilized. The strengths and weaknesses of each test or procedure are discussed and consensus reached whenever possible. If "No consensus" appears in the rating column, reasons for this decision are added to the comment sections.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

ACR Appropriateness Criteria®

Clinical Condition: Staging of Testicular Malignancy

Variant: Testis tumor (diagnosed by orchiectomy)

Radiologic Exam Procedure	Appropriateness Rating	Comments
CT, abdomen and pelvis	9	

Radiologic Exam Procedure	Appropriateness Rating	Comments
X-ray, chest	8	
CT, chest	7	
MRI, abdomen and pelvis	5	Alternative method of imaging nodes if CT is indeterminate
FDG PET	4	
NUC, bone scan	3	
INV, abdomen and pelvis, lymphangiography, bipedal	2	
US, scrotum	2	If questionable for opposite testes
US, abdomen, retroperitoneal	2	
X-ray, abdomen, KUB	1	
X-ray, kidney, intravenous urography, IVP	1	
Appropriateness Criteria Scale 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate		

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Although carcinoma of the testicle is relatively uncommon, representing only 1% of all malignancies occurring in men, it is the most frequent malignancy in men between the ages of 20 and 35 and accounts for 11 to 14% of all deaths due to cancer in the 25 to 34 year age group. The American Cancer Society estimates that in 2005, over 8,000 men will be diagnosed with the disease and that the number of deaths secondary to testicular cancer will be 390.

Over 90% of testicular tumors are of germ cell origin and are malignant. Of these, 40% are seminoma and the nonseminomatous tumors include embryonal cell carcinoma (15-20%), teratoma (5-10%) and choriocarcinoma (less than 1%). Nongerm cell tumors are typically benign and have their origin from the Leydig and Sertoli cells or from connective tissue stroma.

Various staging systems have been used for staging patients with testicular cancer, but most commonly the American Joint Commission on staging and end-results reporting are used.

Testicular tumors are staged as follows:

Primary Tumor (T)

TX Primary tumor cannot be assessed. (In the absence of radical orchiectomy, TX is used).
T0 Histologic scar or no evidence of primary tumor.
Tis Intratubular tumor: preinvasive cancer.
T1 Tumor limited to testis, including rete testis.
T2 Tumor invades beyond tunica albuginea or into epididymis.
T3 Tumor invades spermatic cord.
T4 Tumor invades scrotum.

Lymph Node (N)

NX Regional lymph nodes cannot be assessed.
N0 No regional lymph node metastasis.
N1 Metastasis in a single lymph node, 2 cm or less in greatest dimension.
N2 Metastasis in a single lymph node, more than 2 cm but not more than 5 cm in greatest dimension, or multiple lymph nodes, none more than 5 cm in greatest dimension.
N3 Metastasis in a lymph node more than 5 cm in greatest dimension.

Distant Metastasis (M)

MX Presence of distant metastasis cannot be assessed.
M0 No distant metastasis.
M1 Distant metastasis.

Testicular tumors spread or metastasize by either the hematogenous or lymphatic route. Most follow the regional lymphatic chain alongside the spermatic vessels. Typically, the first order of metastases is the "sentinel" lymph node, which on the left is located at the renal hilar region and on the right in the paracaval region below the renal artery and vein. Left-sided tumors typically spread to the periaortic nodes and preaortic nodes, and right-sided tumors most commonly involve interaortocaval, precaval, and preaortic nodes. Crossover is not uncommon, but typically is from the right to the left. Further drainage is through the thoracic duct, resulting in more widespread metastases.

Tumor Markers

Tumor markers such as alpha-fetoprotein (AFP) and beta human chorionic gonadotropin (B-hCG) are helpful not only in diagnosing patients with testicular tumors but in staging them as well. Approximately 90% of patients with advanced nonseminomatous tumors will have elevated levels of one or both of these markers.

AFP is elevated in approximately 50 to 70% of those with embryonal cell carcinoma, yolk sac carcinoma, or tumors of mixed composition. B-hCG is elevated in 40 to 60% of patients with testicular cancer, including all those with

choriocarcinoma, 80% of those with embryonal cell carcinoma, and 10-25% of those with histologically pure seminoma.

The obtaining of tumor markers before and after orchiectomy is also very helpful in determining whether any residual disease is present and in planning further therapy. Additionally, tumor markers are essential in the follow-up evaluation to assess both the need for and response to therapy (e.g., chemotherapy).

Imaging Studies

Many imaging studies have been used in assessing patients with testicular tumors. In years past, intravenous urography was commonly used for staging purposes; however, with the development of newer techniques the use of this imaging study is of historical interest for this purpose. Studies used today to assess the retroperitoneum include abdominal ultrasonography (US), CT, MRI, and pedal lymphangiography. Studies used to assess pulmonary disease include chest x-ray and chest computed tomography. US continues to be used preferentially for assessing the primary tumors.

Ultrasonography

Scrotal ultrasonography is frequently used in assessing patients with scrotal masses. This study can often differentiate fluid-filled spermatoceles and hydroceles from solid intra-testicular tumors. Oftentimes, the diagnosis is apparent by clinical evaluation, and ultrasound can be used for confirmation and for local staging. The finding of testicular microlithiasis should increase the suspicion of testicular malignancy and if none is found periodic follow-up is recommended.

With the development of newer imaging studies, (e.g., CT) staging with US has found little application in the assessment of patients with some metastatic testicular tumors to the retroperitoneum. Unfortunately, US is operator-dependent, making the uniformity and the reproducibility of the study less than would be desirable. Additionally, because of the interference of overlying intestinal gas and obesity, this study is nondiagnostic in approximately 15 to 17% of patients.

Computed Tomography

Computed tomography is the most common study used for assessing the retroperitoneum for the presence of metastatic testicular malignancy. This study is noninvasive and reproducible and provides excellent imaging of the periaortic and pericaval regions. Difficulties with CT are that many young men have little peritoneal fat, which tends to be an impediment to the study, and that CT cannot detect the presence of metastatic disease in lymph nodes of normal size. Additionally, inflammatory lymph nodes cannot be differentiated from those that are enlarged secondary to malignant disease. CT interpretation is aided by understanding the lymphatic drainage of the testicles. Node involvement is usually limited to the side of the primary tumor, and crossover is usually present only in the presence of advanced disease. Various benign conditions have also been found to mimic metastases from testicular tumors. Lymph nodes larger than 1 cm are suspicious for metastatic disease, particularly if they are located in the hilar

regions of the kidney or in the periaortic or caval areas. Various studies have established the accuracy of CT in detecting metastatic retroperitoneal lymph nodes, which ranges from 73 to 97%. Sensitivity ranges from 65 to 96% and specificity from 81 to 100%. Experience also indicates that accuracy declines in patients with limited disease (stage N1 and stage N2) and also if the upper limit of normal lymph node size is lowered to 4 mm.

Lymphangiography

Lymphangiography is used with decreasing frequency because of its disadvantages, which include its invasiveness, its inability to opacify the sentinel lymph node, and its inability to demonstrate the upper limits of involvement in patients with extensive disease. The accuracy of bipedal lymphangiography has been shown to be comparable to that of CT and varies from 62 to 89%. Sensitivity ranges from 54 to 90% and specificity from 67 to 100%. Studies have also indicated that a combination of lymphangiography and CT improves accuracy, but evidence indicates that this approach is not cost-effective. Magnetic resonance lymphangiography may have potential in the future, but experience is still too limited and the agent, ferumoxtran, has not yet been approved by the FDA for clinical use.

Magnetic Resonance Imaging

Magnetic resonance imaging has also been used in the staging of testicular tumors; however, evidence indicates that it is comparable to CT. MRI does offer an advantage, allowing for the differentiation of blood vessels from lymph nodes, and it may also have the potential of distinguishing residual tumor from fibrosis.

Chest X-Ray

Many studies have addressed the value of chest x-ray in assessing pulmonary metastases. These studies indicate that chest x-ray alone is satisfactory in the initial staging in patients with testicular malignancies. Chest CT offers little in these patients; however, it may offer slight benefit in those with more advanced disease. More recent studies have suggested that initial and recurrent disease in the chest can be detected on chest CT and that routine chest x-rays have a very low yield for early disease and are not considered useful for initial staging for follow-up after therapy.

Radionuclide Imaging

Radionuclide studies have limited value for detecting retroperitoneal metastases. Limited experience with radioimmunoassays for B-hCG and AFP and labeled antibodies to these markers, show promise, but further experience is needed. Gallium scintigraphy has also been used to detect metastatic disease, but clinical experience is limited. Positron-emission tomography (PET) imaging with 2-(F-18)-fluoro-2-deoxy-D-glucose (FDG) has been used in assessing patients with testicular cancers and, though its true value in staging patients has yet to be defined, initial experience has been promising. In initial staging PET has proven only slightly more sensitive than CT. Its use in follow-up for residual masses is more controversial, with some authors recommending it routinely to distinguish mature teratoma from residual disease and others seeing no benefit in assessing

residual masses. The study may be most efficacious for assessing the presence of residual disease after chemotherapy.

Bone scans can be useful in assessing early bone lesions before they are detectable by CT, although one study suggests that FDG PET scans are more sensitive and can substitute for conventional bone scans.

Summary

In most instances, the diagnosis of testicular tumors is established with a carefully performed physical examination and scrotal US. Tumor markers are useful for determining the presence of residual disease, and cross-sectional imaging studies (CT, MRI) are useful in determining the location of metastases. FDG PET scans are have a slightly higher sensitivity than CT, but their role in staging testicular cancer has not been determined in a large study. Bone scans are useful in the absence of FDG PET scans and should be used when there is a suspicion of bone metastases.

Abbreviations

- CT, computed tomography
- FDG PET, Fluorodeoxyglucose positron emission tomography
- INV, invasive
- IVP, intravenous pyelogram
- IVU, intravenous urography
- KUB, kidneys, ureters, and bladder
- MRI, magnetic resonance imaging
- NUC, nuclear medicine
- US, ultrasound

CLINICAL ALGORITHM(S)

Algorithms were not developed from criteria guidelines.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on analysis of the current literature and expert panel consensus.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Selection of appropriate radiologic imaging procedures for evaluation of patients with testicular malignancy

POTENTIAL HARMS

- Computed tomography (CT) accuracy declines in patients with limited disease (stage N1 and stage N2) and also if the upper limit of normal lymph node size is lowered to 4 mm.
- Lymphangiography is used with decreasing frequency because of its disadvantages, which include its invasiveness, its inability to opacify the sentinel lymph node, and its inability to demonstrate the upper limits of involvement in patients with extensive disease.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

An American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologist, radiation oncologist, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those exams generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Choyke PL, Bluth EI, Bush WH Jr, Casalino DD, Francis IR, Jafri SZ, Kawashima A, Papanicolaou N, Rosenfield AT, Sandler CM, Segal AJ, Tempany C, Resnick MI, Expert Panel on Urologic Imaging. Staging of testicular malignancy. [online publication]. Reston (VA): American College of Radiology (ACR); 2005. 6 p. [57 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1996 (revised 2005)

GUIDELINE DEVELOPER(S)

American College of Radiology - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

GUIDELINE COMMITTEE

Committee on Appropriateness Criteria, Expert Panel on Urologic Imaging

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Peter L. Choyke, MD (Review Author and Panel Chair); Edward I. Bluth, MD; William H. Bush, Jr, MD; David D. Casalino, MD; Isaac R. Francis, MD; S. Zafar H. Jafri, MD; Akira Kawashima, MD, PhD; Nicholas Papanicolaou, MD8; Arthur T. Rosenfield, MD; Carl M. Sandler, MD; Arthur J. Segal, MD; Clare Tempany, MD; Martin I. Resnick, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Resnick MI, Amis ES Jr, Bigongiari LR, Bluth EI, Bush WH Jr, Choyke PL, Fritzsche PJ, Holder LE, Newhouse JH, Sandler CM, Segal AJ, Rutsky EA. Staging of testicular malignancy. American College of Radiology. ACR Appropriateness Criteria. Radiology. 2000 Jun;215 Suppl:741-6.

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

ACR Appropriateness Criteria® Anytime, Anywhere™ (PDA application). Available from the ACR Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- ACR Appropriateness Criteria®. Background and development. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

PATIENT RESOURCES

None available

NGC STATUS

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Date Modified: 10/2/2006